PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 November 1999 (15.11.99)	
International application No. PCT/EP98/08568	**Applicant's or agent's file reference** NO 5980/WO
International filing date (day/month/year) 30 December 1998 (30.12.98)	**Priority date** (day/month/year) 18 February 1998 (18.02.98)
Applicant MARK, David, A. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 September 1999 (13.09.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer J. Leitao
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

McCONNELL, Bruce
Avenue Nestlé 55
CH-1800 Vevey
SUISSE

Date of mailing (day/month/year)
15 November 1999 (15.11.99)

Applicant's or agent's file reference
NO 5980/WO

IMPORTANT NOTIFICATION

International application No.
PCT/EP98/08568

International filing date (day/month/year)
30 December 1998 (30.12.98)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address

McCONNELL, Bruce
Société des Produits Nestlé S.A.
P.O. Box 353
CH-1800 Vevey
Switzerland

State of Nationality:
State of Residence:
Telephone No.: +41 21 924 34 17
Facsimile No.: +41 21 924 28 80
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address

McCONNELL, Bruce
Avenue Nestlé 55
CH-1800 Vevey
Switzerland

State of Nationality:
State of Residence:
Telephone No.: +41 21 924 3417
Facsimile No.: +41 21 924 2880
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
J. Leitao
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

- High [illegible] Formula - PEPTAMEN -

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
SOCIETE DES PRODUITS NESTLE S.A.
Attn. McConnell, B.
Case Postale 353
CH-1800 Vevey
SWITZERLAND

02 AOUT 1999

Date of mailing *(day/month/year)* 23/07/1999 ✓	
Applicant's or agent's file reference NO 5980/WO	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/EP 98/08568	International filing date *(day/month/year)* 30/12/1998
Applicant SOCIETE DES PRODUITS NESTLE S.A. et al.	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Maurizio Amodeo

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
NO 5980/WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP98/08568	30/12/1998	18/02/1998
International Patent Classification (IPC) or national classification and IPC A23L1/29		
Applicant SOCIETE DES PRODUITS NESTLE S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/09/1999	04.05.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer ESTANOL, I Telephone No. +49 89 2399 8647

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/08568

I. Basis of th report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-11 as published

Claims, No.:

1-10 as published

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 10.

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate she t

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

s e separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Item III.

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Item V.

Reference is made to the following documents:

D1: US-A-5 340 603
D2: EP-A-0 721 742
D3: US-A-5 221 668

D1 discloses a formula comprising a protein source (e.g. whey) which provides not more than 15% of the calories, a lipid source including a mixture of medium and long chain triglycerides, a carbohydrate source, vitamin C, L-carnitine, taurine, ß-carotene, zinc and selenium. The formula of D1 has a caloric density of 0.8 - 1.2 Kcal/ml (see claims and Tables 3, 4 and 11).

D2 discloses a composition for providing nutrition to an elderly patient comprising a protein source which provides at least 18% of the total calories of the composition, a lipid source including a mixture of medium and long chain triglycerides, ß-carotene, vitamin C, zinc, selenium, taurine and carnitine. The caloric density of the compositions of D2 is 1.2 Kcal/ml (see claims 1-10 and Table on pages 6-8).

D3 discloses a nutritional product for trauma and surgery patients comprising a protein source providing 18%-24% of the calories provided by the product , a carbohydrate source, a lipide source providing 20%-30% of the calories provided by the product, vitamin C (300mg/1500 Kcal), zinc (22.5 mg/1500 Kcal), selenium (70 mcg/1500 Kcal), ß-carotene, L-Carnitine (150 mg/1500 Kcal) and taurine (150 mg/1500 Kcal). The product of D3 has a caloric density of 1.2 to 1.5 Kcal/ml and a calorie to nitrogen ratio of 112.:1 to 145:1. The protein system of D3 comprises lactalbumin hydrolysate, partially hydrolysate sodium caseinate and L-arginine (see claims 1,2,10,11-26 and Tables 1, 2 and 4).

Novelty:
The enteral composition of independent claim 1 is new over the available prior art since it differs (I) from D1 in the provision of energy by the protein source, (ii) from D2 in the caloric density of the composition and (iii) from D3 in the range of energy provision by the protein source. The same applies for independent claim 4 (Article 33(2) PCT).
Claims 2-3 are dependent on claim 1 and claims 5-9 are dependent on claim 4, and as such also meet the requirements of the PCT with respect to novelty.

Inventive step:
The problem underlying the present invention may be regarded as how to provide an alternative enteral nutritional formulation without increased protein levels and high volume of fluid.

The subject-matter of claim 1 or 4 consists in the selection of a percentage provision of energy from the range of 18% to 24% described in document D3. Such a selection can only be regarded as inventive, if the it presents unexpected effects or properties in relation to the rest of the range. However, no such effects or properties are indicated in the application. Hence, no inventive step is present in the subject-matter of claim 1. The same applies for independent claim 4 (Article 33(3) PCT).
Dependent claims 2-3 and 5-9 are only allowable if related to a patentable independent claim (Rule 6.4(b) PCT).

Industrial applicability: The subject-matter of claims 1 to 9 is applicable in the pharmaceutical industry (Article 33(4) PCT).
For the assessment of present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Item VIII.
It seems that in claim 7 the concentration of selenium should read 60 to 90 mcg (see page 6 and 10 of the description).

TENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Articl 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
NO 5980/WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 98/08568	30/12/1998	18/02/1998

Applicant

SOCIETE DES PRODUITS NESTLE S.A. et al.

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. ---

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 98/ 08568

B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 9
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 9 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/08568

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A23L1/29 A23L1/305 A23L1/30 A23L1/09 A23L1/304
A23L1/302

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 340 603 A (NEYLAN MICHAEL J ET AL) 23 August 1994 (1994-08-23) tables 1-4,10,11 column 21, line 47-55	1-3
A	claims	4-9

Y	US 4 112 123 A (ROBERTS WILLARD LEWIS) 5 September 1978 (1978-09-05) column 5, line 9-16	1-3
A	column 6, line 39-50 column 8, line 23-35 claims	4-9

A	WO 97 16079 A (NESTLE SA) 9 May 1997 (1997-05-09) claims; table 11	1-8

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 July 1999	23. 07. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Van Moer, A

2

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 721 742 A (CLINTEC NUTRITION CO) 17 July 1996 (1996-07-17) page 6, line 1 - page 8, line 20; claims	1-8
A	US 5 221 668 A (HENNINGFIELD MARY F ET AL) 22 June 1993 (1993-06-22) claims	1-8
A	US 5 549 905 A (MARK DAVID A ET AL) 27 August 1996 (1996-08-27) column 6, line 5-45	1-8

INTERNATIONAL SEARCH REPORT

[redacted]ation on patent family members

[redacted]ternational Application No
[redacted]T/EP 98/08568

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5340603 A	23-08-1994	NONE	
US 4112123 A	05-09-1978	CA 1088801 A	04-11-1980
WO 9716079 A	09-05-1997	US 5635199 A	03-06-1997
		AU 7294796 A	22-05-1997
		CA 2231525 A	09-05-1997
		CN 1200654 A	02-12-1998
		US 5766621 A	16-06-1998
EP 0721742 A	17-07-1996	US 5589468 A	31-12-1996
		AU 4076595 A	25-07-1996
		CA 2166003 A	14-07-1996
		JP 8231411 A	10-09-1996
		US 5686429 A	11-11-1997
US 5221668 A	22-06-1993	AU 3614393 A	13-09-1993
		CA 2128078 A	02-09-1993
		DE 69325091 D	01-07-1999
		EP 0630181 A	28-12-1994
		JP 2644086 B	25-08-1997
		JP 7500348 T	12-01-1995
		MX 9300999 A	01-09-1993
		NZ 249392 A	26-01-1996
		WO 9316595 A	02-09-1993
US 5549905 A	27-08-1996	NONE	

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(54) Title: CALORICALLY DENSE NUTRITIONAL COMPOSITION

(57) Abstract

An enteral composition and method for providing nutrition to metabolically stressed patients. The enteral composition has an energy density of about 1.4 to 1.8 kcal/ml. The enteral composition includes a protein source providing 15 % to 20 % of the energy of the composition, a lipid source, and a carbohydrate source. The enteral composition has a ratio of non–protein calories per gram of nitrogen of at least about 90:1.

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Calorically Dense Nutritional Composition

This invention relates generally to the treatment and nutritional support of mammals. More specifically, the present invention relates to compositions for use in metabolically stressed patients who need food restriction, but who do not necessarily need increased contents of protein or special nutrients.

Patients suffering from a loss of nutrients require adequate nutritional support. A lack of adequate nutritional support can result in malnutrition associated complications. Thus, the goal of nutritional support is to maintain body mass, provide nitrogen and energy in adequate amounts to support healing, meet metabolic demands characterised by the degree of stress, and support immune function.

A traditional form of nutritional support is administering whole protein liquid feedings to the patient to remedy the protein deficiency. However, some patients requiring nutritional support have a compromised absorptive capacity and thus cannot tolerate whole protein liquid feedings as well as the long-chain fatty acids and complex carbohydrates often present in such whole protein feedings. Many diseases or their consequences can cause malabsorption by impairment of either digestion or absorption. For instance, patients suffering from various types of inflammatory bowel diseases typically cannot tolerate whole protein feedings. As a result, semi-elemental and elemental protein diets were developed to treat such compromised patients.

However, in addition to the traditional inflammatory bowel type patients, semi-elemental and elemental protein diets are currently being used in other patient segments. Specific conditions where these diets are being used include, for example, total parenteral nutrition patients receiving early transitional feedings, acutely ill, and catabolic patients with increased nitrogen needs yet requiring an elemental diet.

Still further, many patients suffering from metabolic stress have a significant need for increased energy but often do not need or tolerate protein levels beyond the normal requirement. Such patients also cannot tolerate the food volume necessary to deliver the energy they need. As a result, such patients need an elemental diet that provides calorically dense nutritional support while at the same time providing moderate non-protein calories per gram of nitrogen. Although a variety of elemental and semi-elemental diets are currently being used in an attempt to treat and/or provide nutritional requirements to such

patients, the needs of the metabolic stressed patients are not being adequately met.

Accordingly, a need exists for an enteral nutritional formulation that meets the nutrient requirements of metabolically stressed patients without unnecessarily subjecting such patients to high fluid volume treatments or formulations with increased protein levels.

In one aspect, this invention provides an enteral composition composition designed for metabolically stressed patients; human and animal. The enteral composition comprises: a protein source providing about 15% to about 20% of the energy of the composition; a carbohydrate source; and a lipid source including a mixture of medium and long chain triglycerides, the enteral composition having a caloric density of at least about 1.4 kcal/ml.

The enteral composition provides nutritional support in the form of increased energy density without elevated protein levels or excess fluid. In particular, the enteral composition, unlike prior compositions, has an energy density of at least about 1.4 kcal/ml.

Preferably, the enteral composition provides energy dense nutritional support while at the same time providing moderate non-protein calories per gram nitrogen (NPC/gN). Specifically, the enteral composition has a clinically acceptable ratio of non-protein calories per gram nitrogen of at least approximately 90:1; for example about 140:1 to about 100:1.

In an embodiment, the hydrolysed protein source is hydrolysed whey protein.

In another aspect, this invention provides an enteral composition for a metabolically stressed patient comprising: about 15% to about 20% of the energy of the composition of partially hydrolysed whey protein; a carbohydrate source; and a lipid source including a mixture of medium and long chain triglycerides; the composition having an energy density of at least about 1.4 kcal/ml and a ratio of non-protein calories per gram of nitrogen of at least about 90:1

In another embodiment, the lipid source of the composition includes at least 70% medium chain triglycerides.

Moreover, due to the calorically dense nature of the enteral composition, the enteral composition may include 100% of U.S. RDA of vitamins and minerals in about 1500 kcal (1000 ml).

Preferably, the composition is in ready-to-use form, is nutritionally complete, and contains proteins, lipids, vitamins and minerals in proportions

suitable for older children (10+ years) and adults. The enteral composition may be fed by tube or orally.

The invention also provides a method for providing nutrition to a metabolically stressed patient. The method includes administering to the patient a therapeutically effective amount of a composition having an energy density of at least about 1.4 kcal/ml. The composition with such increased energy density includes a protein source comprising approximately 15% to 20% of the energy of the composition, a carbohydrate source, and a lipid source including a mixture of medium and long chain triglycerides.

The composition is be especially useful for patients using the composition as a supplement (i.e. HIV, cystic fibrosis) and as a nocturnal feeding (cystic fibrosis).

Additional features and advantages of the invention are described in, and will be apparent from, the detailed description of the presently preferred embodiments.

Nutritional support of hospitalised as well as non-hospitalised patients requires prevention, recognition and treatment of nutritional depletion that may occur with illness. The goals of nutritional support include stabilising metabolic state, maintaining body mass, and/or facilitating growth in the presence of disease and gastrointestinal dysfunction.

Certain disease states exist that alter intake, absorption or metabolism. For example, certain health conditions can impair the nutrient absorption and/or reduced gastrointestinal tolerance for diets which are based on whole proteins. These conditions include patients suffering specifically from a compromised gut function as well as patients, due to the severity of their condition, who are simply unable to tolerate whole protein diets.

Moreover, although certain patients with impaired nutrient absorption and/or reduced gastrointestinal tolerance may need fluid restriction, such patients do not necessarily need the increased contents of protein or special nutrients often present in existing elemental diets. For instance, patient groups suffering from Crohn's disease, cancer, cystic fibrosis, short bowel syndrome, cerebral palsy, intractable diarrhoea, gastric reflux and HIV/AIDS often are classified as falling within this group of patients. Likewise, patients transitioning from parenteral feeding, are acutely ill, or are considered post-surgery with cardiac/renal complications requiring fluid control also have a need for increased energy, but often do not need or tolerate protein levels beyond normal

requirements and cannot tolerate the fluid volume necessary to deliver the needed energy. For purposes of the present application, this population of patients are generically referred to as metabolically stressed patients.

This invention provides a product that is specifically directed to meet the nutritional needs of metabolically stressed patients without elevated protein levels or excess fluid. To this end, the invention provides calorically dense nutritional support in the form of an enteral composition while at the same time providing a moderate NPC/gN ratio. The composition preferably utilises hydrolysed whey protein, medium chain triglycerides and maltodextrin to enhance absorption in the metabolically stressed patients.

The protein source provides approximately 15% to 20% of the total energy of the composition; for example about 15% to 18%. In an embodiment, the protein source comprises approximately 16% (4 g/100 kcal) of the total energy of the composition. For adults and older children (10+ years old), the protein concentration is optimal for the moderate tissue repair needs of the targeted patient populations without imposing an undue nitrogen burden on renal function.

The composition is preferably a peptide-based diet to maximise tolerance and absorption. In an embodiment, the protein source includes enzymatically hydrolysed whey protein. In a preferred embodiment, the protein source is hydrolysed whey protein. This type of protein source reduces the incidence of gastric reflux because gastric emptying is faster than with diets containing casein or whole whey.

Also, the hydrolysed whey protein serves as a rich source of the amino acid cysteine. Cysteine is a limiting amino acid for the formation of glutathione, and endogenous glutathione needs are greater in patients with chronic inflammatory and infectious conditions. The composition preferably contains approximately 0.1% to 0.8% of energy as cysteine. In a preferred embodiment, the composition contains approximately 0.37% of energy as cysteine (925 mg/1000 calories).

The protein source may also include a portion as free amino acids. As with protein hydrolysate, the use of free amino acids reduces the potential for nutrient malabsorption. In an embodiment, the protein source contains from about 0.1% to 2.0% of energy of free amino acids. Preferably, the protein source of the present invention contains less than about 2% of energy of free amino acids.

Carbohydrates provides, in an embodiment, approximately 35% to 65% and, most preferably, approximately 40% to 60% of the energy of the composition. In an embodiment, the carbohydrate source provides about 51% of the energy of the composition. A number of carbohydrates may be used. By way of example, the carbohydrates can be chosen from maltodextrin, corn starch, sucrose and corn syrup solids.

The lipid source may includes a mixture of medium chain triglycerides (MCT) and long chain triglycerides (LCT). The lipid source invention provides about 20% to about 50% of the energy of the composition; preferably about 25% to about 40%. In an preferred embodiment, the lipid source provides about 33% of the energy of the composition.

The lipid profile is designed to meet essential fatty acid needs (omega-3 and omega-6) while also keeping the medium-chain triglyceride (MCT) content high and long-chain triglyceride (LCT) content low compared with prior formulas. Preferably, the lipid source comprises approximately 30% to 80% by weight MCTs. In a preferred embodiment, the lipid source includes about 70% by weight from MCTs. MCTs are easily absorbed and metabolised in the metabolically stressed patient. The use of MCTs will also reduce the risk of potential for nutrient malabsorption. In a preferred embodiment, the medium chain triglyceride source is fractionated coconut oil.

The remainder of the lipid source is a mixture of LCTs. Suitable sources of LCT's are canola oil, corn oil, soy lecithin and residual milk fat and soybean oil. The lipid profiles containing such LCTs are designed to have a polyunsaturated fatty acid omega-6 (n-6) to omega-3 (n-3) ratio of about 1:1 to 10:1; preferably about 6:1 to about 9:1. The proposed ratio of n-6:n-3 is designed to reduce the immune suppression associated with high omega-6 fatty acid concentration and provide adequate essential fatty acid. In an embodiment, the composition includes an omega-6 to omega-3 ratio of about 7:1.

Still further, the composition contains a specialised vitamin and mineral profile. The composition may include at least 100% of the United States Recommended Daily Allowance (USRDA) of vitamins and minerals in 1500 kcal. Moreover, the composition includes higher levels of key vitamins and minerals designed to support the metabolically stressed patients.

Specifically, the composition may include a high level of zinc. Preferably, at least approximately 225% of the USRDA of zinc is provided in the composition per 1500 Kcal. In an embodiment, 28.5 to 43.5 mg per 1500

calories of zinc are provided. In a preferred embodiment, 36 mg per 1500 calories of zinc is provided. The increased zinc compensates for zinc losses and provides increased zinc for tissue repair in a patient having increased healing requirements.

The composition may also include an increased amount of vitamin C. At least approximately 750% of the USRDA of vitamin C is provided per 1500 Kcal. In an embodiment, 405 to 615 mg per 1500 calories of vitamin C is provided. In a preferred embodiment, 510 mg per 1500 calories of vitamin C is provided. Vitamin C is believed to accelerate the healing and granulation in patients with severe healing requirements. Vitamin C will support increased requirements/losses after surgery.

The composition may also include increased amounts of selenium. Selenium deficiencies may develop in patients having elevated healing requirements. At least approximately 60 to 90 μg of selenium may be provided in 1500 calories of composition. In a preferred embodiment, approximately 75 μg of selenium per 1000 calories is provided.

Many of the commercially available enteral formulas contain far below the amount of carotenoids (beta-carotene) found in usual diets of normal healthy people. In fact, patients on liquid formula diets as their sole source of nutrition for one week or more have been found to have plasma concentrations of carotenoids of only 8% to 18% as compared to controls consuming a free choice of diet (Bowen et al, "Hypocarotenemia in Patients Fed Enterally with Commercial Liquid Diets," *Journal of Parenteral and Enteral Nutrition*, 12(5): 44-49 (1988)). Those on enteral formulas for more than three weeks have negligible concentrations of any common serum carotenoids.

To meet these requirements, the composition may include a source of β-carotene. β-Carotene is added to the composition to normalise beta-carotene serum plasma levels and to avoid beta-carotene deficiency in long term tube-fed patients. β-Carotene also meets a portion of the required Vitamin A, thereby meeting micro-nutrient requirements in a small caloric volume. Moreover, β-carotene is an important nutrient with anti-oxidant properties. The composition may include approximately 1.25 to 4.0 mg per 1500 kcal of β-carotene. In a preferred embodiment, the composition includes approximately 1.52 mg of β-carotene per 1500 kcal of the composition. This amount prevents deficiencies and provides for possible increased requirements in the healing patient.

Moreover, the β-carotene and vitamin A levels allow plasma concentrations of retinol to be increased to near normal optimal levels of 500 mcg per litre.

The composition may also include increased amounts of L-carnitine and taurine to support the increased requirements of the acutely ill, catabolic patient. Both taurine and L-carnitine are preferably present in amounts of approximately 120 to 180 mg per 1500 calories. In preferred embodiments, both taurine and L-carnitine are present in an amount of approximately 150 mg per 1500 calories.

Still further, the composition may include decreased amounts of magnesium. Magnesium has been associated with diarrhoea. In an embodiment, magnesium is present in an amount of approximately 308 mg to 462 mg per 1500 calories. In a preferred embodiment, magnesium is present in an amount of approximately 400 mg per 1500 calories.

The composition may be in any suitable form such as ready-to-use liquid form and powder form. The composition can provide the total nutritional requirements of the metabolically stressed patient or can act as a supplement. The composition can be tube-fed to a patient, or fed by having the patient drink it. For instance, the composition can be provided in cans or a spike and hang bag. The composition is preferably ready-to-use and does not require reconstitution or mixing prior to use.

Unlike prior formulations, the composition provides calorically dense nutritional support while at the same time providing a moderate NPC/gN ratio. To this end, the composition preferably has a caloric density of approximately 1.4 to 1.8 kcal/ml. For example, the composition has a caloric density of about 1.5 kcal/ml. The composition provides a moderate NPC/gN ratio of at least about 90:1. For example, the composition provides a NPC/gN ratio of about 140:1 to about 100:1. Preferably, the composition provides a NPC/gN ratio of 131:1.

Furthermore, unlike prior formulations, the composition has a low osmolality of approximately 375 to 600 mOsm/kg H_2O in an unflavoured product. The osmolality of the composition in a flavoured product is approximately 500 to 700 mOsm/kg H_2O.

The composition may be utilised to treat metabolically stressed patients. As used herein, metabolically stressed patients are patients who, due to either a disorder or condition, are unable to tolerate whole protein diets and need fluid restriction, while at the same time cannot tolerate elevated protein levels or excess fluid. For example, the composition may be utilised to provide nutrition

to critically ill patients transitioning from total parenteral nutrition therapy and acutely ill, catabolic patients. Moreover, the composition can be utilised to provide nutrition to patients suffering from the following conditions and/or diseases; Crohn's disease; cystic fibrosis; HIV/AIDS; cancer; patients of post-surgery with cardiac/renal complications requiring fluid control; intractable diarrhoea; short bowel syndrome; cerebral palsy; and gastric reflux.

Of course, it will be appreciated that a variety of compositions are possible. An example of a composition has a caloric density of about 1.5 kcal/ml. This is equivalent to 375 kcal/250 ml which will, in a preferred embodiment, be one unit (can or container) of product.

Example 1

The composition includes the following ingredients: water; maltodextrin, enzymatically hydrolysed whey protein, medium-chain triglycerides (MCT source: fractionated coconut oil); corn starch; soy bean oil; soy lecithin; potassium phosphate; guar gum; calcium citrate; sodium phosphate; choline chloride; sodium chloride; calcium phosphate; calcium ascorbate; magnesium chloride; potassium citrate; magnesium oxide; potassium chloride; taurine; citric acid; L-carnitine; zinc sulphate; ferrous sulphate; DL-alpha tocopherylacetate; nicotinamide; retinyl palmitate; calcium pantothenate; manganese sulphate; copper sulphate; pyridoxine hydrochloride; riboflavin; thiamine; folic acid; cholecal ciferol; biotin; potassium iodide; β-carotene; sodium molybdate; chromium chloride; phylloquinone; sodium selenate; and cyanocobalamin.

The composition may have the following nutrient composition (per 1500 calories (1000 ml)):

Nutrient Composition	Amount	% U.S. RDA*
Protein	60.0 g	132
Carbohydrate	191.0 g	**
Lipid***	58.5 g	**
Water	780 ml	**
Vitamin A	6000 IU	100
Beta-Carotene	3.0 mg	**
Vitamin D	600 IU	148
Vitamin E	45 IU	148
Vitamin K	75 mcg	**
Vitamin C	510 mg	840
Thiamine (B_1)	3.0 mg	200
Riboflavin (B_2)	3.6 mg	212
Niacin	42 mg	208
Vitamin B_6	6 mg	300
Folic Acid	810 mcg	136
Pantoth. Acid	21 mg	140
Vitamin B_{12}	12 mcg	132
Biotin	600 mcg	132
Choline	675 mg	**
Taurine	150 mg	**
L-Carnitine	150 mg	**
Calcium	1000 mg	100
Phosphorus	1000 mg	100
Magnesium	400 mg	100
Zinc	36 mg	240
Iron	27 mg	148
Copper	3.0 mg	148

Nutrient Composition	Amount	% U.S. RDA*
Manganese	4.0 mg	**
Iodine	225 mcg	148
Sodium	1020 mg	**
Potassium	1872 mg	**
Chloride	1740 mg	**
Chromium	60 mcg	**
Molybdenum	180 mcg	**
Selenium	75 mcg	**

* U.S. Recommended Daily Allowance for Adults & Children 4 or more years of age

** U.S. RDA not established

*** MCT provides 40.8 grams/1000 ml

In this example, the protein source comprises essentially 100% hydrolysed whey protein. The carbohydrate source preferably includes approximately 70% to 95% maltodextrin, from about 5% to 15% corn starch, and up to about 20% sucrose; all % being on the basis of energy. Lastly, the lipid source preferably includes approximately 70% MCTs, approximately 17% soybean oil; approximately 8% residual milk fats; and approximately 5% soy lecithin; all % being on the basis of weight.

Example 2

The composition of example 1 is evaluated in a group of severely traumatised patients requiring early enteral feeding. Patients are fed by small bowel feeding tubes. The goal of this early feeding is to supply at least 60% of their calculated energy needs. The primary data collected to evaluate this early feeding is to determine the tolerance to early and fairly aggressive feeding. Gastrointestinal symptoms such as diarrhoea, bloating and cramping are tabulated and evaluated. Actual intake as a percentage of calculated energy requirements is calculated for each patient on each day of feeding for five

consecutive days. The nutritional goals set are 25 kcal/kg of estimated body weight/day and 1.6 grams of protein/kg/day.

Eighteen (18) patients are entered into the study and 16 of these patients complete the 5 days of feeding. For the first 24 hours of feeding, the average intake for the 16 patients is 65 ± 12% of the calculated nutritional requirement. The intake over the first 48 hours of feeding is 68 ± 8% of requirements. Over the first 72 hours of feeding, the average intake is 73 ± 6% of requirements and for the first 96 hours of feeding, the mean intake typically rises to 87 ± 6% of requirement. Over the full five days of feeding evaluation, the average intake is 92 ± 7% of the calculated energy requirements for the 16 patients who completed the full study period. Diarrhoea develops in only one patient in the group and this generally persists for approximately 18 hours. No other gastrointestinal symptoms would typically be reported during the study period.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

Claims:

1. An enteral composition designed for metabolically stressed patients comprising:

a protein source providing about 15% to about 20% of the energy of the composition;

a carbohydrate source; and

a lipid source including a mixture of medium and long chain triglycerides, the enteral composition having a caloric density of at least about 1.4 kcal/ml.

2. The enteral composition of claim 1 wherein the composition provides a ratio of non-protein calories per gram nitrogen of at least approximately 90:1.

3. The enteral composition of claim 1 or claim 2 wherein the protein source consists essentially of partially hydrolysed whey proteins.

4. An enteral composition for a metabolically stressed patient comprising:

about 15% to about 20% of the energy of the composition of partially hydrolysed whey protein;

a carbohydrate source; and

a lipid source including a mixture of medium and long chain triglycerides;

the composition having an energy density of at least about 1.4 kcal/ml and a ratio of non-protein calories per gram of nitrogen of at least about 90:1.

5. The enteral composition of any of claims 1 to 4 wherein the lipid source provides about 20% to 50% of the energy of the composition.

6. The enteral composition of any of claims 1 to 5 which includes at least about 100% of U.S. RDA of vitamins and minerals in about 1500 kcal.

7. The enteral composition of any of claims 1 to 5 wherein the composition includes per 1500 kcal of composition:

a zinc source providing from approximately 28.5 to 43.5 mg;

a vitamin C source providing from approximately 405 to 615 mg;

a selenium source providing from approximately 60 to 90 mg;
a taurine source providing from approximately 120 to 180 mg; and
a L-carnitine source providing from approximately 120 to 180 mg.

8. The enteral composition of any of claims 1 to 7 further including a source of β-carotene.

9. The enteral composition of any of claims 1 to 8 which has an energy density of about 1.4 to about 1.8 kcal/ml.

10. A method for providing nutrition to a metabolically stressed patient comprising the step of administering to the patient a therapeutically effective amount of a composition comprising:

a protein source comprising approximately 15% to about 20% of the energy of the composition;

a carbohydrate source; and

a lipid source including a mixture of medium and long chain triglycerides, the enteral composition having a caloric density of at least about 1.4 kcal/ml.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/08568

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A23L1/29 A23L1/305 A23L1/30 A23L1/09 A23L1/304
A23L1/302

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 340 603 A (NEYLAN MICHAEL J ET AL) 23 August 1994 (1994-08-23) tables 1-4,10,11 column 21, line 47-55	1-3
A	claims	4-9

Y	US 4 112 123 A (ROBERTS WILLARD LEWIS) 5 September 1978 (1978-09-05) column 5, line 9-16	1-3
A	column 6, line 39-50 column 8, line 23-35 claims	4-9

A	WO 97 16079 A (NESTLE SA) 9 May 1997 (1997-05-09) claims; table 11	1-8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 July 1999	23. 07. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Van Moer, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/08568

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 721 742 A (CLINTEC NUTRITION CO) 17 July 1996 (1996-07-17) page 6, line 1 - page 8, line 20; claims	1-8
A	US 5 221 668 A (HENNINGFIELD MARY F ET AL) 22 June 1993 (1993-06-22) claims	1-8
A	US 5 549 905 A (MARK DAVID A ET AL) 27 August 1996 (1996-08-27) column 6, line 5-45	1-8

2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

[redacted]national application No.
PCT/EP 98/ 08568

Box I Observations where c rtain claims w re found unsearchable (Continuati n of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 9
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 9 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5340603 A	23-08-1994	NONE	
US 4112123 A	05-09-1978	CA 1088801 A	04-11-1980
WO 9716079 A	09-05-1997	US 5635199 A	03-06-1997
		AU 7294796 A	22-05-1997
		CA 2231525 A	09-05-1997
		CN 1200654 A	02-12-1998
		US 5766621 A	16-06-1998
EP 0721742 A	17-07-1996	US 5589468 A	31-12-1996
		AU 4076595 A	25-07-1996
		CA 2166003 A	14-07-1996
		JP 8231411 A	10-09-1996
		US 5686429 A	11-11-1997
US 5221668 A	22-06-1993	AU 3614393 A	13-09-1993
		CA 2128078 A	02-09-1993
		DE 69325091 D	01-07-1999
		EP 0630181 A	28-12-1994
		JP 2644086 B	25-08-1997
		JP 7500348 T	12-01-1995
		MX 9300999 A	01-09-1993
		NZ 249392 A	26-01-1996
		WO 9316595 A	02-09-1993
US 5549905 A	27-08-1996	NONE	